although by nature the very antithesis of myself, was a good friend. In the opinion of many he was harshly treated by the world for holding views that did not conform to standard. Perhaps this very world has become more tolerant than it was in Creighton's time, because even in his own subject there are epidemiologists who express with impunity to-day views as heterodox as those for which Creighton was pilloried and ostracised 40 years ago."

F. H. GARRISON.

ANIMAL RESERVOIRS OF HUMAN DISEASE WITH SPECIAL REFERENCE TO MICROBIC VARIABILITY *

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The subject assigned me, I take it, is to give you a brief summary of those human diseases which we owe to animal life and which the physician is apt to encounter from time to time in his practice or discover in the hospital and dispensary. In more general terms, I am to discuss the pathological relations between the human and animal species. Leaving aside acute poisoning due to the sting of certain insects and the bite of serpents, these relations are limited largely to the transfer or interchange of infectious and parasitic organisms. Two main groups of diseases spring from this relationship:

a. Infectious and parasitic organisms producing self-perpetuating diseases in animals may at times and under certain circumstances gain a foothold in the human subject. These diseases are as a rule not transmitted from one human being to another, either because the virus is not eliminated or else the mode of infection is peculiar. Or again, the highly developed sanitary environment of patients may prevent such transfer. Among these diseases may be mentioned anthrax, rabies, tuberculosis, Malta

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fever, tularemia, melioidosis, glanders, Rocky Mountain spotted fever, streptotoccus infections, various tapeworm diseases, and trichinosis.

b. Diseases due directly to biting insects and arachnids. They comprise a formidable group which hovers forbiddingly over immense areas of the world's surface otherwise highly desirable for civilized man. In addition to the major plagues such as malaria, yellow fever, typhus, sleeping sickness, and trench fever, there are various minor diseases due to insects. It may seem somewhat strained to call these animal diseases yet such they are. The protozoan parasites which they inject into the human subject belong primarily to the insects and arachnids. In them the important sexual stages for the perpetuation of the species go on. The human host is a convenient secondary culture medium for the multiplication of the vegetative stages giving rise to a large asexual progeny which withdrawn into the insect goes through the maturing sexual stages. Some of these protozoa have through this procedure sacrificed the capacity of independent existence in the insect owing to their parasitic or semiparasitic reliance on the human subject. Nevertheless all zoological evidence points to insects as the real, primary hosts. This second group of diseases I shall not further discuss, since it forms the material on which tropical medicine is built.

The animals which contribute to human disease may be divided into useful and noxious species. From a scientific viewpoint the distinction is of no value. It becomes, however, very significant when we endeavor to suppress the diseases. We may make continuous, relentless warfare on rats and mosquitoes, but the problem becomes more complex when we deal, for example, with cows as reservoirs of human diseases. Medical literature abounds in references to the possibilities of harm lurking in animal diseases, and in nearly every great epidemic of the past, animal diseases have been reported as precursors. Bold inferences were drawn from mere relations in time and space and fanciful theories have had their days, such as the one that bovine

tuberculosis was human syphilis in the cow. With the coming of scientific medicine animal diseases have taken their proper place in etiology and it may be said that in spite of our intimate association with animal life, either through direct contact, as in farm life, or indirect through foods and other animal products, and in spite of the large number and variety of infectious and parasitic diseases belonging to every species of domesticated and wild animal, so far as the latter are known, very few are transmitted to man. In fact we have only an odd lot of diseases to consider. Nevertheless they are formidable, and unheeded and neglected they would give the human race many unexpected jolts from time to time.

With one exception the diseases to which I shall refer briefly tend to occur either sporadically or in small groups. They first come to the attention of the practising physician. One acquainted with the chief clinical manifestations of these diseases may well score a point if he should be able to make an early diagnosis. Such diagnosis will be frequently tentative because a final decision will depend on bacteriological and serological tests. To direct the investigation into the right channels means half the battle won. To-day such diseases, after they have been identified, usually come under the jurisdiction of the health officer who endeavors to trace the source of the infection and eliminate it if possible. Diseases of this class new to a given region are usually ranged under some known disease at first and the erroneous diagnosis often carried along for months before it is rectified.

The object of a lecture of this kind is not fulfilled by simply detailing what is already recorded in medical writings but to point out relationships and possibilities still hidden in the future. To do this we necessarily enter the field of speculation. I think that there is perhaps too little rather than too much speculation in medical discussions to-day. The one condition not often met is that to look into the future we must be firmly planted in the present. To provide a basis for such speculation I shall briefly

give the salient characteristics of the important diseases that come within the scope of our subject.

Glanders is a dangerous and frequently fatal disease, sporadically encountered in man, which is exclusively carried by diseased horses and their relatives, the asses and mules, although it is inoculable into a large number of other animals. Before the entrance of the automobile into industrial life, glanders was not uncommon. In fact twenty-five years ago there was a fair amount of this disease traveling daily over our city streets. It caused the death of a number of scientists and their helpers in the laboratories. Medical literature is replete with details of cases in men in contact with diseased horses. The open disease in horses is readily diagnosed and the earliest stages brought out by mallein. Health boards were quite alert in stamping out the disease by killing open cases and watching those which reacted to mallein. To-day it is fairly well suppressed, thanks to the diminution of horses and the activities of Health agencies. In man the disease takes on protean characteristics from chronic lesions of the skin lasting twenty years to acute septicemic cases fatal in a few weeks. It has been repeatedly and thoroughly monographed in medical serial publications so that there is no difficulty in getting acquainted with the human side of the disease.

Bubonic and pneumonic plague. The relation of rats and certain rodents to bubonic and pneumonic plague was established fully a generation ago. Since then sporadic outbreaks of this disease have made themselves felt in widely separated territories, and during such occurrences, plague rats have regularly been found in the infected territory. In the far west of the United States other rodents, such as ground squirrels, have been found dangerous carriers. The microbe is one of a large group infesting the respiratory tract of the lower animals but singled out by its fierce onslaught on the human species. It is well known that the bubonic form of plague is not readily passed from man to man, probably owing to the fact that the mode of

introduction of the human virus into a fresh wound would rarely occur. The diseased rat aided by the bite of the rat flea provides the necessary mechanism between rat and man. On the other hand the pneumonic form may be transmitted like other respiratory infectious agents directly. Originally derived from a rodent of woodchuck type, it becomes a genuine human plague. The Black Death of the Middle Ages is generally identified with the pneumonic type of plague.

Malta or undulant fever. Since the great war attention has been called by clinicians to an affection appearing in our midst sporadically and usually in isolated cases which is characterized by prolonged fever without recognizable local manifestations. Its similarity to Malta fever, traced by Bruce and co-workers nearly forty years ago to goat's milk around the Mediterranean where this beverage is used extensively in place of cow's milk, has been emphasized. From the greater number of recent cases a bacillus has been obtained from the blood which closely resembles *Bacillus melitensis,* or *Brucella* as it has been recently renamed in honor of Bruce, the first to cultivate the organism from the goat. In 1918, Alice Evans while studying the bacteria in cow's milk showed that *B. melitensis* was closely related to *B. abortus* from the cow. Although the former had been isolated in 1889 and the latter, by Bang, in 1897, the close relationship of the two was not pointed out until twenty years later. This condition may be ascribed to the fact that the two streams of information resulting from investigations in human and animal pathology rarely mingle.

The appearance of an undulant type of fever in man in our midst associated with an organism up to the present not distinguishable by routine bacteriological and serological methods from either *B. melitensis* or *B. abortus* raises many important problems which cannot be reviewed at this time and which demand more detailed study. The situation may be briefly defined as follows. There are at present three different hosts of *Brucella,* the goat, the pig

and the cow. The bovine organism has been thoroughly studied; the pig organism much less thoroughly. The goat organism, known to exist among goats in southern Europe and in several southern states in this country, is still to be comparatively studied, as coming directly from goat's milk. Only through an extensive comparative investigation of these three races of *Brucella* will the problem of human undulant fever be solved. Among fifteen human strains so far examined I find at least three varieties and none agreeing in all cultural characters with the bovine type. It may be claimed that the latter is modified by passage through man, but in default of the actual human experiment, this gap in our knowledge can only be filled by continued cumulative study of accessible material. The burden of proof still rests upon those who claim that the bovine type of *Brucella* produces undulant fever in man. Bacteriologists working with cultures of Malta fever are frequently laid low with the disease in spite of the usual care observed in bacteriological laboratories. On the other hand *B. abortus* from the cow has been under investigation for more than a quarter century the world over without being suspected of producing any febrile conditions in laboratory workers who have not protected themselves in any special manner. Moreover veterinarians coming directly in contact with the diseased tissues in their daily practice have not presented any grievances against the bovine bacillus.

In 1912 Whitmore, an Englishman working in the Far East, called attention to a bacillus which may be destined to play an important role in world history. The bacillus has characters reminding one in turn of the typhoid bacillus, of proteus and of glanders, but it is not like any of these. It may be a highly generalized type from which those mentioned have sprung. Since 1912, the disease it induces has been encountered spontaneously in rats, guinea-pigs, rabbits, cats, dogs and a horse. Up to 1924, the human disease was localized in Rangoon, Burma, and the Straits Settlement. Fifty cases have been studied, of

which forty-eight have died. The two survivors are chronically diseased. The human disease resembles in some respects acute septicemia or cholera or glanders, according to the cases observed. Diagnosis was made in most instances after death, since the cases were regarded as known human diseases during life. Owing to the variety of localizations the bacillus has been isolated from sputum, local ulcers, urine and the blood during life. The rat may be the true carrier and disseminator.

Tularemia. This disease has been the theme of a recent lecture by Dr. Edward Francis who has devoted much attention to a study of its distribution in the United States and the modes of transfer. I am therefore restricting my remarks to some of the salient points in its natural history. It is essentially a disease of rodents and was discovered in 1912 by Drs. McCoy and Chapin in California ground squirrels. Two years later Wherry and Lamb described the first case in man. In 1919, Dr. Francis studied a small group of cases in farmers, in Utah, and traced the infection to jack rabbits. He also showed the ready transmissibility of the virus through the mechanical agency of various insects and mites living on or drawing blood from diseased animals. The clinical manifestations following infection consist of inflammation and suppuration of the regional lymph nodes, and fever lasting some days and after an intermission returning. Convalescence is slow. The mortality may be high in certain outbreaks. Laboratory workers are prone to contract the disease. The disease has been reported from all parts of the United States and is generally due to handling the carcasses of wild rabbits, such as skinning and preparing them for food. Within a few years, several cases of the human disease have been reported from Japan and the disease identified by Francis as tularemia.

Rat-bite fever. This disease has been definitely associated with the bite of rats in widely separated countries, among them Japan, Mexico, Scotland and the United

States. The wild rat during the biting introduces into the wound a spirillum, possibly also other organisms, in the saliva. The disease in man is characterized by a relapsing type of fever with an inflammatory reaction round the wound, enlargement of regional lymph nodes, and a macular, erythematous eruption. The clinical reports vary in details and minor particulars but fundamentally they are alike. The spirillum when inoculated in infected blood multiplies in the rat, guinea-pig and rabbit. In the rat and guinea-pig conjunctivitis and keratitis are observed and it has been suggested that the saliva of the rat is infected by the conjunctival discharges.

Infectious jaundice or Weil's disease. We are indebted to the rat for another characteristic human disease, which like rat-bite fever has a world-wide distribution. Infectious jaundice has played a prominent role among soldiers in various wars of the 19th century. The relation of the rat to this disease and the causal agent, a spiral organism, *Leptospira icterohemorrhagiae* were demonstrated by Japanese scientists in 1916. The disease is characterized by sudden onset of fever, severe muscular pains, and jaundice usually on the fourth day. Hemorrhages are usually present. Albuminuria is frequently observed. A second elevation of temperature, known as after-fever, may occur after subsidence of the first febrile reaction.

The foregoing group of disease, although differing widely etiologically, have in common the sudden onset with fever. They also are blood diseases in so far as the infectious agent may be recovered from the blood during life. Localizations, either primary or secondary, are frequent, and when primary, the regional lymph nodes are involved. The mortality is low, if we except melioidosis in which it appears to be very high. There is furthermore the relapsing character of the fever common to most of them. The entire symptomatology indicates a lack of stability of the microörganism in the foreign host, accompanied however

with a high invasiveness and persistence. Widely different from one another are the following highly important animal diseases transmissible to man:

Anthrax. The anthrax bacillus has always been a classic to the bacteriologist since it was the first microbe actually seen in the blood of affected animals and also the one with which Koch over fifty years ago began his career and Pasteur gained recognition through his now celebrated anthrax vaccine. The disease is always treated in clinical and pathological texts and I need not delay on it. The bacillus is quite a universal agent, since it attacks horses, sheep, and cattle, and perhaps many wild species on pastures. The dangerous factor in its makeup is the spore which survives in a dry condition many years. I have myself kept dried spores eight years and found them making abundant growth overnight when placed in suitable culture media. The wool, hairs, bristles and hides of domestic animals are dangerous vehicles of these spores and governments have been trying for many years to devise successful disinfectants which will not materially injure these articles of commerce and industry. Inasmuch as there is no evidence that healthy animals carry the infectious agent the danger to human beings is very slight, provided the governments do their duty in not allowing the products coming from animals dead of anthrax to enter commerce at all or at least without adequate disinfection.

Rabies, like anthrax, has a wide spread among animal victims and almost all mammals tried have been found inoculable. The real distributors, however, are limited to the species that bite, the dog and wolf. Casual transmission by other rabid animals may occur through their saliva but this is rare. There is no other disease known with such inclusive powers to infect and cause fatal disease. Here also Pasteur's genius has provided a defense in his method of vaccination. The increasing extent and intensity of rabies among dogs in densely populated territories over the entire globe have stimulated efforts to provide some protective measures for dogs with a modified

Pasteur vaccine. Such procedure is now being tried in certain communities but without the scientific centralized oversight which such an important practical experiment demands. The great international importance of rabies is expressed in the International Conference on Rabies held in Paris in 1927, during which all the various procedures used on human patients were discussed and scrutinized.

Paratyphoid diseases. Another widespread group of bacteria producing septicemic and enteric diseases in animals and not infrequently group outbreaks in man is the paratyphoid group including *B. enteritidis,* related on the one hand to the typhoid bacillus, on the other to certain races of *B. coli.* In man this species of bacteria is most frequently associated with acute gastrointestinal upsets, leading in rare instances to a fatal outcome. In another group of cases the disease simulates typhoid but is less severe, less protracted and rarely fatal. Where man acquires this infection has been the subject of research for nearly forty years and enquiries are still going on. The reasons are not far to seek. The paratyphoid group of bacteria produces enteritis in cattle and swine, and abortion in mares. It produces epidemics among rabbits, guinea-pigs and mice in our laboratories, and in wild rats. It is represented by several distinct serologic groups which break up into minor subgroups. In the smaller animals several races may infest the same species at the same or different times. Certain group outbreaks in man have been definitely traced to rats and to veal, horseflesh and pork, when not sufficiently cooked. It is not improbable that the strains infesting the larger animals are distinct from one another but that the smaller animals are susceptible to all. It may be that the rat is an exception and cultivates its own variety. The difficulty with the mass of researches upon the paratyphoid races has been too great attention to nondescript cultures with no history and too little to the larger animal hosts.

Tuberculosis. So much has been written during the past twenty-five years on the significance of bovine tuber-

culosis to the human race that I can add little to the subject not already well known. The transmission of the bovine tubercle bacillus occurs almost exclusively in cow's milk. In the second and more advanced stages of the disease, the udder may become the seat of tuberculous processes due to the escape of bacilli temporarily circulating in the blood as the result of some focus breaking down. About one to two per cent of tuberculous cows have some tuberculous foci in the udder. Cows in very advanced stages of the disease, when emaciation has set in and the disease has become generalized, may discharge a few bacilli in the udder. The cow's chief form of tuberculosis is pulmonary. The cow coughs up particles of caseous material and mucus impregnated with tubercle bacilli. This coughed-up material is chiefly swallowed but some is thrown out during coughing, otherwise it would be difficult to account for the preponderating pulmonary disease of the cow herself. The swallowed bacilli are discharged in the feces and when the milking is not guarded by preliminary cleansing of the cow, some of these bacilli may find their way into the milk pail with fecal matter. This source of bacilli cannot be significant owing to various inhibiting conditions. It has, however, not been quantitatively studied.

The main points upon which agreement is general are that children under five are almost the only victims, that the cases of subcutaneous lymph node tuberculosis due to the bovine bacillus are relatively benign, and that, according to a careful study of the statistical evidence of Cobbett, between five and six per cent. of all deaths from tuberculosis are attributable to the bovine virus. In view of the data on hand, pasteurization of milk is gradually being introduced in large cities. Fortunately, the thermal death point of tubercle bacilli is low. The eradication of bovine tuberculosis is now being pushed by State and Federal activities in the hope of establishing permanently tuberculosis-free areas and gradually increasing such areas until the disease has been eliminated. The method used is to kill all animals reacting to tuberculin and repeating

the procedure every six months until reactors are no longer encountered. The entire movement is tedious, expensive, and fraught with difficulties tending towards relapses. These are attributable to failures of the tuberculin, carelessness in administering the test and in interpreting results, introduction of infected animals, and reintroduction of the virus from feed, swine, dairy products and the like. Although the problem of bovine tuberculosis may be considered temporarily and practically disposed of by the use of pasteurized milk and the continued killing of tuberculin-reacting bovines, the scientific aspects are not so satisfactorily cleared up. The reason for the immunity of the human adult is not in sight since many must be exposed in cow stables to bovine bacilli. The existence of atypical forms as described by Griffiths needs more detailed study. Some method of recognizing the presence of the bovine type in the human body would be of great value to the clinician and surgeon.

Rocky Mountain Spotted Fever. A disease of startling possibilities but restricted by advancing agriculture is the Rocky Mountain spotted fever which first came to the notice of medical science in the nineties of the last century. Since then numerous papers have been published by various investigators and some very valuable data brought to light. The human disease is an acute febrile disease, characterized by an eruption of spots, varying much according to the severity of the attack from bright red to purple and becoming petechial in character. The mortality is high. In 1903, 121 cases had been collected, of which 84 were fatal. The immediate incitant is a tick, the bite of which injects the virus. This mode of transmission accounts for the non-contagiousness of the human disease, observed by all local physicians. The demonstration of the infectivity of the wood tick was given by Ricketts in 1906. He also was able to induce the disease in guinea-pigs which animals in turn infected ticks placed on them. He furthermore showed that the virus may pass to the ova of the infected female tick and thence to the next generation. Ten years later, Wolbach demonstrated the presence of minute

bacteria-like organisms in the vascular lesions of human and animal victims and in the infecting tick. In 1923, Noguchi showed the prophylactic efficacy of a serum produced in rabbits with the blood of infected guinea-pigs.

Thus it appears that it required about a quarter century to round out more or less our knowledge of this unique disease. According to the data at hand, the tick harbors certain Rickettsia-like organisms to which it is indifferent. They are highly specialized parasites transmissible through the ovum to the next generation. More likely the virulence of the infecting agent is maintained through the agency of wild animals, such as mountain goats, woodchucks, spermophiles and others, which act as temporary reservoirs of virus for the tick. Whether the tick is self-sustaining as to the virus or whether it depends on these various animal hosts for a fresh supply of virus, in either case we have to deal with a distinctly animal disease and it is therefore included in this survey.

Septic sore throat. Our relation to animal life under the present urban and rural conditions of living is made quite intimate through the consumption of raw cow's milk. I have already mentioned the presence of tubercle bacilli in tuberculous udders and of *B. abortus* in the udders of a small per cent. of cows which have aborted at some time and are carriers of this species. A third potentially dangerous organism appears now and then in the udder—a streptococcus—which has been the cause of numerous large and small epidemics of septic sore throat. The sudden appearance of widespread epidemics of septic sore throat was signalized some twenty years ago. Before that time this disease was probably prevalent in small outbreaks and such occurrences had been reported from England by Klein, Savage and others. In this country the consolidation of distributing agencies and the practice of mixing the milk of a large number of cows led to the larger outbreaks. Hundreds and even thousands of cases in a single epidemic have been reported since 1910 in different cities of the United States.

The continuance of the epidemics in spite of increased sanitary precautions and restrictions made it necessary to reject the current explanations that the milk had been infected in transit by human beings. Working upon Massachusetts outbreaks some fifteen years ago with J. H. Brown, I formulated the theory that some streptococcus alien to the cow had entered and multiplied in the udder for a more or less indefinite period. Unknown to us, Savage, in England, had expressed the same idea in the course of his work. At the same time D. J. Davis, studying outbreaks in Chicago, came to the same conclusion. Since then many outbreaks have been investigated and the views presented have been sustained. The hemolytic streptococci of septic sore throat are not identical with ordinary hemolytic streptococci of the cow's udder, but evidently alien to it, either producing severe mastitis or else simply multiplying in the udder and causing only slight disturbances. They are to all appearances of human derivation, since identical strains have been found in the throats of the dairy workers in most of the large outbreaks. Only through a very careful bacteriological control of the streptococci occurring in any dairy herd can similar calamities be prevented in the future among those drinking raw milk.

Certain species of bacteria, common to both man and animals, have received as yet little attention. I refer to the many races of *B. coli,* streptococci and staphylococci, parasitic on mucous membranes of domestic animals. To the urban dweller only those contaminating raw foods are of significance. It remains for the future to see them serologically typed and compared with forms found in man in diseased conditions. Those parasitic in the udder of the cow have already been referred to as probably harmless to man if we except the *Streptococcus epidemicus* just referred to.

Animal parasites. This review would be quite incomplete if I failed to mention certain higher animal parasites either shared in common by man and certain animals, or

else transferable from animals to man. Certain tapeworms have figured conspicuously in the past in those countries where certain kinds of meat are eaten raw. Thus the beef tapeworm lives in the human intestine in the adult form and in muscular tissue of cattle in the larval or cysticercus stage. The pork tapeworm enjoys the same dual hospitality in man and the pig. When human beings eat the cysts in raw or underdone beef or pork, the intestines may become the seat of the respective tapeworm. The fish tapeworm, not infrequently encountered in eastern Europe, has probably established itself recently in some of the inland waters of the United States. Carried across in the intestines of some European immigrant and discharging countless ova, the parasite thus furnished the opportunity for fishes to become infested with the intermediate or larval stage. Another tapeworm (echinococcus) belonging in its adult, intestinal stage to the dog has figured more or less in the medical and surgical literature of the past because the intermediate larval stage following the ingestion of ova discharged by the dog has been found in almost every organ of the human body, notably the liver in which organ large cysts develop gradually. These may break and when situated in vital spots, such as the medulla oblongata, they have caused instant death.

Another strictly animal parasite which has played a conspicuous role in human pathology in the past, especially in central Europe, is the roundworm, *Trichinella spiralis.* It has caused extensive local epidemics with high mortality following the consumption of the raw muscular tissue of a single pig. Trichinosis is not unknown even today when unfortunates consume inadequately cooked pork. The parasite is attributed to the pig, but it occurs in rats and small laboratory animals have been infected successfully. All that is necessary to maintain the disease is for the pig to eat an infected rat and for another rat to gnaw the body of the infected dead pig and so on *ad infinitum.*

Having catalogued briefly most of the conspicuous maladies which we derive from animal reservoirs, it may be

worth while to pass in review the animals themselves. Here our division into useful and noxious may be followed. The cow has been responsible for the beef tapeworm, certain types of paratyphoid infection, tuberculosis, septic sore throat, and very doubtfully for cases of undulant fever. Anthrax cannot be charged to the cow exclusively, since it attacks other domestic animals. Hides may carry spores, however, and permanently infect grazing lands irrigated by water from tanneries and other factories working up hides, wool, hair and bristles. Sheep are of relatively little significance as carriers of human disease if we except wool impregnated with anthrax spores. Swine are responsible for trichinae, the pork tapeworm, paratyphoid infections and probably certain forms of undulant fever. Though they are victims of bovine tuberculosis whenever exposed, it is doubtful that human beings, excepting perhaps butchers, are infected from pork owing to inspection in large cities, the freedom of muscular tissue from foci and the general custom of cooking pork. Horses are the source of glanders, of anthrax in horse hair and hides and possibly of certain races of paratyphoid. Dogs are responsible for rabies and the echinococcus tapeworm.

Among the noxious mammals, rats stand at the head, as potential reservoirs of bubonic plague, of the spirilla of rat-bite fever and melioidosis, as well as the spirochæte of infectious jaundice, and certain races of paratyphoid bacilli. Mice, as the most domestic of noxious pests, are minor reservoirs of plague bacilli, of certain skin affections, and being subject to various paratyphoid infections, potential reservoirs of these as well. Among game we are aware of the wild rabbit as carrier of the tularemia virus, sphermophiles of plague when endemic, and of various species of game as sources of the Rocky Mountain spotted fever virus.

If we now reverse the emphasis of our theme and ask how many human diseases are transmitted to animals there is very little to discuss. If a disease passed from animal

to man becomes independent of the animal source and self-perpetuating by direct transfer from man to man, then we may say that such disease is again transmissible back to animals. This would be true for pneumonic plague in which the sputum becomes infectious for other human beings. However, very few of the human cases of disease described as originating in animals have been shown to be dangerous to their environment. Among them septic sore throat, glanders, discharging tuberculous lymph nodes containing bovine tubercle bacilli, groups of paratyphoid and meat poison cases discharging bacilli in the feces may perhaps transmit enough infectious material to produce clinical cases. On the whole medical literature contains very little evidence of such occurrences. In view of the sanitary isolation of patients practised to-day any escape of infectious material is largely prevented under current conditions of hospital and private practice. What would happen if human beings lived the natural life of animals might be quite different from present actualities. We are thus compelled to admit that apparently animals do not suffer from strictly human diseases. The current is plainly the other way. Even the ubiquitous human tubercle bacilli are traceable to tuberculous lesions in only a few species of animals, notably monkeys, interned in zoological gardens. Most animal tuberculosis is due to the bovine bacillus. Poultry which is the victim of a special form of tuberculosis plays only a very insignificant role in the human disease.

Underlying this phenomenon of the passing of infectious agents from animals to man and the reverse is the far more important and fundamental one as to the fate of such aberrant parasites. Do they become modified in the human or other aberrant host in one passage? Is the process irreversible? Bearing on this question it is of interest to note that the guinea-pig, the most useful laboratory animal, is victimized by a number of diseases which may have been derived at least in part from close association with man. Among the more significant are two paraty-

phoid diseases, a pneumonia due to an atypical pneumococcus, a streptococcus producing polyadenitis, and a respiratory affection associated with types of *B. mucosus capsulatus*, also known as Friedländer types. These are all self-perpetuating diseases in the guinea-pig and the respective bacteria are probably derived from man but are modified and no longer transmissible to man.

The most important of the probable transformations of human viruses in animals is that of cowpox or vaccinia. Much has been written upon the original source of vaccine virus. Since the day of Jenner, who considered cowpox as a derivative of grease of the hock in horses, there has been more or less fluctuation of opinion as to the nature of cowpox itself. The findings of the celebrated Lyons Commission in 1865 controlled for a long time the views of the medical profession. This commission, while admitting that smallpox virus may be successfully inoculated into the cow, denied that it underwent any mitigation or modification, and that, returned to man, it would produce genuine smallpox. Since that time a number of investigators have succeeded in transmitting smallpox to the cow and producing genuine cowpox, and it is now quite generally regarded as a derivative of smallpox. The frequent appearances of cowpox in the early years of the nineteenth century were in all probability due to the accidental inoculation of the cow with smallpox or with vaccine from the hands of the milker, which in its turn was at some earlier time derived from smallpox by passage through the cow. Vaccine, derived from variola, the so-called variola-vaccine, was prepared by Voigt, of Hamburg, in 1881 and used by him with success. Later a new stock of variola-vaccine was prepared successfully in Munich, Bavaria. A few years ago, horsepox, appearing in Holland during the World War, was successfully transmitted by de Jong to calves. The eruption from the latter produced typical vaccine vesicles on the arms of children and a subsequent inoculation with ordinary cowpox was abortive. There is thus a close immunological reciprocity between smallpox,

cowpox and horsepox which indicates that they may have been originally derived from the same ancestral type.

Preceding the introduction of solid culture media by Robert Koch, and therefore preceding the beginnings of bacteriology as a science, there were current more or less fantastic ideas of the variability of microörganisms which if accepted would have negatived the possibility of recognizing any definite etiological factors in infectious diseases. Hence with the introduction of methods to test these current ideas the relative stability of bacterial species was soon universally accepted. This salutary change was not without certain disadvantages for it put off the study of variability many years. In human medicine this disadvantage played only an insignificant role since the first pathogenic species to be discovered were usually invasive forms and quite stable. To those who studied disease from a comparative standpoint with an abundance of material, variations promptly presented themselves, especially among paratyphoid strains, among glanders and among tubercle bacilli. Even in the strictly human camp violent controversies arose over the significance of variants in the etiology of Asiatic cholera. Since then every conceivable species of bacteria capable of growing on artificial substrates has been found to be made up of a group of variants. The variations were grounded either in slight differences as to fermentative capacities, pigment and capsule production, or in varying capacities to produce toxins or to respond to immune bodies. Even the latest subject of research, the streptococcus associated with scarlet fever, is found endowed with slightly varying characters.

Among the invisible filterable causes of disease the determination of cultural and physiological variants is at present impossible owing to the fact that artificial culture in the bacteriological sense is not yet attained. But even in this group two immunologically different races have been found in the virus of foot-and-mouth disease. Smallpox prevails under the guise of the usual form and a milder type, alastrim. Numerous illustrations might be given,

involving practically every human and animal disease studied, of the universal occurrence of variant types.

That there are numerous physiological differences and diversities among the races of man and animals upon which the microörganism parasitize is so well known that I merely mention it. The differences are accentuated when several host species of animals are inoculated with the same microörganism. Then also there are discovered certain peculiar, accidental relationships among hosts which a given virus might utilize. Thus the house mouse is not susceptible to glanders but the field mouse is. Mouse septicemia bacilli are quite virulent for pigeons. In fact all that has been stated in this lecture serves to illustrate both host specificity and the occasional breakdown of this barrier.

Going parallel with observations in natural disease, laboratory studies by many scientists extending over many years have brought to light fluctuations, modifications, mutations and dissociations of physiological and morphological characters of bacteria as well as increase or decrease in virulence through serial passages through animals. In spite, however, of these changes, suggesting both degeneration and regeneration, and the sudden appearance of hitherto latent characters, the different cultivable species of bacteria remain true to a certain fundamental type within which the variations occur. This leads us to the concept of microörganisms as possessed of a number of more or less independently variable characters, morphological and physiological, some of which may be augmented, depressed, or lost, or even appear as new characters. Among the pathogenic forms the increase in toxin production, the appearance of defensive envelopes may modify disease. In fact there are probably multiple toxins of different activities as well as multiple types of defense, each brought into action by certain specific, but accidental, host relations, making possible new diseases whenever the special relationship is tapped by the accidental meeting of certain hosts and certain microörganisms. Thus *B. abortus*

from the cow, passing to swine and remodeled in this species, may accidentally pass back into the cow's udder as pathogenic for some human beings.

Taking these facts into consideration and the increasing number of new trials open to microbes to become established in new hosts made possible by the continuous flux of an increasingly dense population of both human and animal species, domesticated or merely parasitic on conditions produced by domestication, we may begin to visualize the possibilities for new diseases to appear. They may come more or less suddenly when conditions are rapidly altered as in war for man, and in rearing large numbers of animals in confinement with regular and frequent communication with other similar populations. We may readily conceive of the many changes in infectious organisms partly accomplished, followed by the destruction of the new race because some conditions are not fulfilled, and hence the many failures which precede what we may call the birth of a new disease. In this highly significant process the original character of the aberrant parasite may be so altered that its source cannot be traced. Its course may have been devious and the intermediate stages unobserved when they occurred and since wiped out, so that this course can no longer be traced back to its beginnings. The appearance of apparently new diseases associated with ultramicroscopic organisms is particularly mysterious, since our methods are quite inadequate to inform us from what direction the newcomer hailed. The ancestry may be directly before us, in our midst, in fact in some animal disease, but we may fail to see it because of the irreversible process that has brought the change about. With this concept in mind we can imagine many dangerous combinations frustrated, cut short, by hygiene and sanitation, numerous diseases in gestation prematurely aborted, but occasionally one successfully escaping destruction and launched into the world, at first unrecognized until a certain momentum has been acquired which brings the disease into the open.